REMARKS/ARGUMENTS

Claims 39-47, 49-52 and 55-58 are pending in this application. Claims 39-47, 49-50 and 52 have been amended for clarity to remove references to figures. Although the prior rejections under 35 U.S.C. §101 and obviousness-type double patenting were withdrawn, all claims are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement and written description. All rejections are respectfully traversed.

Rejections Under 35 U.S.C. §112, First Paragraph - Enablement

Claims 39-47, 49-52 and 55-58 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the enablement requirement.

Utility has been asserted for PRO335 as an immunostimulator for use in the treatment of diseases benefiting from the enhancement of immune response such as AIDS and further, for antagonists of PRO335 as immunosuppressors in graft-vs-host disease, autoimmune disease, etc. based on the positive result in an MLR assay. This utility pertains to the field of immunotherapeutics. The Examiner states that the MLR assay is not predictive of *in vivo* efficacy, and hence undue experimentation would be needed to use the invention. Applicants respectfully disagree. Just because experimentation maybe needed to practice the invention, such experimentation is not necessarily undue, and further, it does not mean that the art of immunotherapeutics as a whole is unpredictable. In fact, Applicants submit that the level of skill in the art of immunotherapeutics is very advanced that the skilled artisan would find that the experimentation needed in this instance, routine. In *In re Wands*, the courts concluded that the amount of experimentation needed was not undue in view of the direction and guidance provided by the Appellants and the level of skill in the art:

> "the court held that ....there was 'considerable direction and guidance' in the specification; there was 'a high level of skill in the art at the time the application was filed;' and all the methods needed to practice the invention were well known." 858 F.2d at 740, 8 USPQ2d at 1406; M.P.E.P. 2164.01(a)

The MLR assay is widely used and is considered a standard assay for testing drug candidates that are potential immunomodulators. Based on the positive MLR result of

PRO335, Applicants' have created a reasonable expectation that PRO335 or its antagonists can be used *in vivo* for immune related conditions. While the outcome of *in vivo* tests is not certain, experimentation may be necessary to achieve a positive result, and the amount of such experimentation is not undue. In this regard, Applicants respectfully remind that the skilled artisan in the field of Immunology and Immunotherapeutics at the effective filing date (September 17, 1998), would likely be a person with a Ph. D. or M.D. degree, sometimes both and with extensive experience. Such a person would, in fact, find it routine to carry out *in vivo* analysis to determine whether PRO335 or its antagonists are useful in *in vivo* immune diseases, based on such directed guidance.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Rejections Under 35 U.S.C. §112, First Paragraph - Written Description

Claims 39-43, 52, and 55-58 are rejected for lack of written description for variants of the disclosed sequence. According to the rejection, Applicants' amendment incorporating a functional limitation is not sufficient to overcome this rejection, "because the functional limitation is not considered to be a definite use of the polypeptide for the reasons set forth above."

Applicants submit that whether a specification shows that Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including level of knowledge and skill in the art, and teaching provided by the specification. The inventor is not required to describe every single detail of his or her invention; an Applicant's disclosure obligation varies according to the art to which the invention pertains. The present invention pertains to the field of recombinant DNA technology. It is well established that the level of skill in this field is relatively high, and is represented by a Ph.D. scientist having several years of experience in the pertinent field. Accordingly,

the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made.

The present invention concerns isolated nucleic acids having 80%, 85%, 90%, or 99% sequence identity with a nucleic acid sequence encoding a disclosed polypeptide sequence, with a functional limitation wherein the claimed polypeptide "induces proliferation of stimulated T lymphocytes in a mixed lymphocyte reaction". Besides disclosing the full-length native human PRO335 nucleic acid, the specification provides further details about the cloning and expression of variants of the polypeptide PRO335 (see, *e.g.*, pages 112-117), and the design of DNA primers for isolating associated polynucleotides (see page 184-185 of the specification). Additionally, the information provided from page 30 onwards refers to PRO335 as possessing leucine rich repeats, a conserved structural element, and having homology to known proteins in the leucine rich repeat superfamily such as LIG-1, ALS (see specifically page 31, line10). Thus, structural features of the protein variants were clearly envisioned in this disclosure. The specification also discloses that screening methods for leucine-rich proteins were known in the art at the time of filing: "Examples of screening methods and techniques are described in the literature (see, Klein et al....; U.S. Patent No. 5,536,637), page 31, line 13. Thus, the specification provides sufficient information about structural characteristics of the variants in the claimed genus and further demonstrates how these variants could be isolated. Case law and the Written Description Training Materials clearly acknowledge that the written description requirements can be met by a combination of structural and functional characteristics shared by members of the genus, as is done in the present case. Thus, the skilled artisan would reasonably conclude that Applicants had possession of the claimed polypeptides at the effective filing date.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any additional fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-1618 P2C79**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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By: Daphne Reddy
Daphne Reddy (Reg. No. 53,507)

HELLER EHRMAN WHITE & McAULIFFE LLP
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

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